sponse to administration of edrophonium chloride (Tensilon),[2,3] others[4] have reported a positive response. This patient's abscess was incised and drained and a specimen of abscess cultured, but because there was a response to edrophonium chloride (Tensilon), radical debridement was delayed several days. Subsequent serum toxin studies were only strongly suggestive, but not diagnostic, of type A botulism, because detection of toxin in serum is most likely when studies are done closer to the onset of clinical symptoms.[3] In this particular patient the delay in diagnosis caused delay in obtaining serum for toxin studies. Subsequent mouse inoculation showed sublethal but clinically consistent illness in mice unprotected by monovalent type A antitoxin.

Disease entities of low incidence are not often considered in the early stages of a clinical syndrome. When clinical features of botulism are present in the absence of an implicated food product, clinicians should not be lured away from the diagnosis of wound botulism when a positive edrophonium chloride test (Tensilon) might suggest otherwise.

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Chronic Arsenic Poisoning Masquerading as Pernicious Anemia

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ARSENIC POISONING is a malady of protean manifestations that can affect the neurologic, hematologic, dermatologic and gastrointestinal systems.[1-3] A patient's presentation may be confusing, but the correct diagnosis, if considered, can be suggested by a simple, rapid, inexpensive and noninvasive screening procedure.

Report of a Case

A 64-year-old Hispanic man was admitted to another hospital because of two weeks of worsening mid and left upper quadrant abdominal discomfort. He had a history of mild adult-onset diabetes mellitus, but otherwise had no significant illnesses and was taking no medicines. He said he did not use alcohol excessively. Physical examination on admission showed no abnormalities.

Laboratory studies disclosed the following values: hematocrit, 29%; mean corpuscular volume, 91 cu μm, and leukocyte count, 1,900 per μl, with 48% neutrophils, 2% band cells and 43% lymphocytes (the rest of differential and platelet count not provided). A bone marrow aspirate and biopsy specimen showed megaloblastic changes, pronounced erythroid hyperplasia and a full range of myeloid maturation. These findings were interpreted as consistent with folate deficiency, and a regimen of low-dose folic acid replacement was begun pending blood levels and further evaluation.

No response was generated by the therapy. After several days in hospital, the patient began to have paresthesias in his hands and feet and difficulty walking. Neurologic examination at that time showed a profound loss of vibratory sense and proprioception in all four extremities and near-absent deep tendon reflexes. Although the folic acid and vitamin B_{12} concentrations in the patient's serum were in the low-normal range and no macrocytosis was noted on the peripheral blood smear, it was felt by the staff, in consultation with the hematology department, that this picture was most typical of pernicious anemia. A lumbar puncture showed no abnormalities except for mildly increased cerebrospinal fluid protein content. The first part of a Schilling test was done, which showed a decreased excretion of 2.6%. This result was interpreted as confirming the presence of pernicious anemia. Vitamin B_{12} was administered every other day, 1,000 grams intramuscularly, with five doses given before discharge. Because of the patient's continuing vague abdominal symptoms, other diagnostic procedures were done during his 16-day hospital stay—abdominal ultrasound, intravenous pyelogram, liver-spleen scan and barium enema. The only abnormal findings were decreased gastric motility and mild splenomegaly.

Upon discharge, the patient's anemia and neutropenia had substantially decreased, but his neurologic state was essentially unchanged. The discharge diagnosis was "probably pernicious anemia with severe neurologic manifestations."

One week after discharge, the patient presented to this hospital because of persistent abdominal pain and continued neurologic deterioration. He was unable to walk and barely able to stand. He also had near anesthesia in his hands, increasing muscular weakness and an inability to concentrate at times. On physical examination a hyperpigmented band was seen on his trunk and he had hyperkeratotic palms with several small, hyperpigmented macules on the digits. His fingernails appeared normal. There was a considerable loss of vibratory, proprioceptive, light touch and pinprick sensation distal to the elbows and knees, with a milder deficit extending to the trunk. His hand grip and wrist extension were significantly diminished in strength on both sides and he was barely able to lift his legs when

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supine. His stance was unsteady and he was unable to walk unaided. Deep tendon reflexes of the lower extremities were absent and those of the upper extremities were diminished.

A complete blood count showed a hematocrit of 33%, hemoglobin of 11.2 grams per dl and a leukocyte count of 4,900 per μl with 68% neutrophils, 4% band cells, 19% lymphocytes, 5% monocytes and 4% eosinophils. Platelet estimate was normal. Aliquots of urine were sent for heavy metal and porphyrin screens. The next day the test was reported as positive for heavy metals and suggestive of arsenic. A 24-hour urine specimen had an arsenic concentration of 0.55 grams per ml (normal <0.02 μg per ml, according to the Hine Laboratories, San Francisco). Lead and mercury concentrations were normal. For diagnostic confirmation, a large lock of scalp hair was shaved and sent for analysis in five sections. The most proximal section contained 45 μg per gram of arsenic (normal <0.3 to 0.5 μg per gram) and the distal sections were all within normal limits. These data suggested that the poisoning had occurred within four to five weeks, which is the average amount of time for 1 cm of hair growth, assuming a typical average daily growth of 0.35 mm.[4]

Both the peripheral blood smear and the bone marrow biopsy specimen from the other hospital were reviewed by our pathologists, who felt that all of the changes seen, including basophilic stippling on the peripheral smear and megaloblastoid forms, karyorrhexis and binucleated erythrocyte precursors in the marrow, were entirely consistent with the hematologic effects of arsenic.

Within six days of admission, the patient had been started on chelation therapy. He received 200 mg of dimercaprol intramuscularly every four hours for two days and was then changed to D-penicillamine, 250 mg given by mouth every eight hours. The urine was monitored for arsenic, which rapidly cleared within five days.

Although the patient felt better during his hospital course, there was little objective evidence of improvement. Electromyographic studies obtained several days after admission showed a polyneuropathy, with denervation limited primarily to the distal leg muscles. He received physical therapy in addition to medical treatment and was discharged to a nursing home for extended care. The source of the arsenic poisoning was not determined. Neither the home nor workplace showed any obvious environmental source, and the patient said he had not been exposed to pesticides or herbicides, contaminated seafoods, copper-smelting operations or wood preservatives. He took no home remedies or tonics and drank no illegal whiskey ("moonshine"). Attempted homicide was suspected but not proved.

Six months after discharge, the patient showed considerable improvement. He regained his ability to walk, but only with a wide-based gait. He still exhibited bilateral weakness of wrist and hip flexion and of foot dorsiflexion. Diminished sensation, particularly in the hands, persisted.

Discussion

Because of the multisystem involvement of chronic arsenic poisoning, the differential diagnosis is large and includes vitamin B_{12} deficiency, acute febrile polyneuritis (Guillain-Barré syndrome), Addison's disease, porphyria and poisoning from other heavy metals, particularly thallium.[1,2] The appearance of the peripheral blood smear in arsenic poisoning differs in several important ways from that in vitamin B_{12} or folic acid deficiency. In vitamin B_{12} deficiency, the erythrocytes are primarily normocytic and normochromic, and basophilic stippling is common; hypersegmented neutrophils are absent or rare, and relative eosinophilia may be seen. The bone marrow in arsenic poisoning may show occasional megaloblastoid forms but more typically is characterized by karyorrhexis and binucleated erythrocyte precursors.[2] All of these hematologic abnormalities except eosinophilia were present in our patient.

The neuropathy of subacute combined degeneration of the spinal cord that results from vitamin B_{12} deficiency may closely mimic that of chronic arsenic poisoning—that is, general weakness, glove-and-stocking paresthesias, loss of vibratory and position senses, unsteady gait and diminished deep tendon reflexes (initially).[5] A lack of parallelism between the hematologic and neurologic manifestations may arise from this vitamin deficiency. In our patient, however, the normal serum concentration of vitamin B_{12} and the normal mean corpuscular volume in the presence of profound hematologic and neurologic abnormalities could have suggested the correct diagnosis.

Summary

Except for the absence of white transverse bands on the fingernails (Mees' lines), this patient presented the classic signs of chronic arsenical poisoning—gastrointestinal complaints followed by profound peripheral neuropathy and concomitant hematologic and dermatologic changes. Because early, aggressive treatment with chelating agents may alleviate the effects of this toxin, a prompt diagnosis might substantially affect a patient's short and long-term prognosis.[3,6] This case shows the value of screening for heavy metals in evaluating gastrointestinal symptoms that are accompanied by pancytopenia or neurologic abnormalities.

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